

### **REMARKS**

Applicants have elected Group I, Claims 1-32 and the combination of SEQ ID NO's: 146, 148, 149, 166, 167, 178, 194, 199, 200, 207, 285, 347, 424, 489, 505, 509, 516, 519, 532-534, 542, 545, 551, 529, and 14, 15, 25, 28, 30, 42, 44, 47, 52, 61, 62, 71, 558, 555. The office Action is drawn to these claims and SEQ ID NO's. Claims 33-39 have been withdrawn as being directed to non-elected subject matter. Applicants hereby reserve the right to pursue the subject matter of the canceled claims in one or more divisional patent applications.

Applicants are herewith filing a 37 CFR § 1.132 (herein referred to as a "Rule 132 declaration " attached as Exhibit A, signed by the inventors. The declaration addresses the scope of enablement and the differences between the instant invention and the cited reference.

### ***Drawings***

The Examiner has objected to Figure 9 as unreadable because the boxes are too dark. Applicants here with submit a correct Figure 9 in compliance with 37 C.F.R. § 1.121(d). In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant objection.

### ***Claim Objections***

Claims 1-32 are objected to because of informalities. Specifically, the Examiner has objected to the SEQ ID NO's: as listed and requires correction of the claims to indicate which combination of SEQ ID NO's are used to detect estrogen and androgenic activity. In response, Applicants have amended claims 1-6, 12, 15-19, 23, 24, 26 and 32 to indicate the combination of SEQ ID NO's used to detect each activity. Claims 7 and 20 have also been amended to identify the combination used to detect estrogen and androgenic activity. No new matter has been added by virtue of this amendment and its entry is respectfully requested.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant objection.

***Claim Rejections Under 35 U.S.C. § 112- Scope of Enablement***

Claims 1-7 and 10-32 are rejected under 35 U.S.C. § 112, first paragraph. The Examiner asserts that the specification while being enabling for a method of detecting estrogenic or androgenic activity in a sample comprising sheepshead minnow or large mouth bass fish cells, the specification is not reasonably enabling for any type of fish species or detection of genes partially encoded. Applicants respectfully traverse.

Applicants describe the estrogenic/androgenic agents. See, for example page 17, lines 15-25. Applicants further describe the methods of detecting expression of genes in response to these agents. See, for example, page 17, lines 15-31 through to 21, lines 1-10 and the examples which follow. Furthermore, since these compounds affect hormonal activity by binding to the estrogen and/or androgen receptor, the same genes would be activated in all types of fish. Applicants also describe that since hybridization (as is well-known to one of ordinary skill in the art, does not generally require 100% complementarity) these sequences can bind to variants as long as they have some sequence similarity. See, for example, page 10, lines 1-31 and page 12, lines 26-31 through to page 13, lines 1-11 which describe various hybridization stringency. For example, Table 1 includes genes like apolipoprotein E, alpha tubulin, ATPASE 6; Table II includes genes like cytochrome c oxidase, glutathione peroxidase III, alpha tubulin, LDL receptor, cathepsin B, ubiquitin; Table III includes, *inter alia*, genes from different species like cytochrome b, perforin-1 (human); prostaglandin D synthase (*X. laevis*), complement C3 (*P. olivaceus*). Thus, Applicants disclose identification of genes from different species or easily identifiable and known genes that are up- or down regulated using the combination of SEQ ID NO's disclosed herein. One of ordinary skill in the art would have not require anything further other than obtaining samples from various fish and testing the response to various agents using the instant invention.

Applicants herewith attach Exhibit A, a Rule 132 Declaration showing results that the sequences can be used in other species.

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In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

***Claim rejections- 35 U.S.C. § 112-Written Description***

Claims 1-7 and 10-32 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Applicants respectfully traverse.

Applicants provide a detailed analysis of regulated genes. See, for example Tables I-III, wherein Applicants provide a list of genes which are regulated, the location, the gene identification and E-score. A person of ordinary skill in the art could easily identify which of these genes would be up- or down regulated in any fish in response to the estrogen and/or androgenic agents based on the instant specification. For example, Table 1 includes genes like apolipoprotein E, alpha tubulin, ATPASE 6; Table II includes genes like cytochrome c oxidase, glutathione peroxidase III, alpha tubulin, LDL receptor, cathepsin B, ubiquitin; Table III includes, *inter alia*, genes from different species like cytochrome b, perforin-1 (human); prostaglandin D synthase (*X. laevis*), complement C3 (*P. olivaceus*). The sequences disclosed by Applicants have identified genes which are regulated in response to the estrogenic and/or androgenic agents. Since these genes, see for example Tables I-III, were identified using the SEQ ID NO's disclosed in the instant specification, Applicants submit that the same genes can be identified in any fish species.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

***Claim Rejections Under 35 U.S.C. § 102***

Claims 1-7, 9-24 and 30-32 are rejected under 35 U.S.C. § 102(b) as being anticipated by Larkin *et al.* (*Marine Environmental Research* 2002 Volume 54 p. 395).

Applicants respectfully traverse. Applicants invention is directed in part to a method for detecting the presence of an agent having estrogenic or androgenic activity in a sample, the by analyzing a fish cell for expression of at least one gene encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO's: 146, 148, 149, 166, 167, 178, 194, 199, 200, 207, 285, 347, 424, 489, 505, 509, 516, 519, 532-534, 542, 545, 551, 529 for identifying estrogen activity and SEQ ID NO's: 14, 15, 25, 28, 30, 42, 44, 47, 52, 61, 62, 71, 558 and 555 for identifying androgenic activity.

Larkin *et al.*, do not teach, disclose or anticipate **any of the disclosed sequences**; does not teach or disclose **specific combinations of sequences**; does not teach or disclose whether an agent induces estrogenic or **androgenic** activity in a sample; does not teach or disclose **which SEQ ID NO's** would identify an agent having **estrogenic or androgenic activity**. Furthermore, Larkin *et al.*, do not teach any of the above spotted onto arrays, using a nylon membrane as an array for attachment of any one of the sequences or combinations thereof to identify estrogen and androgen activity; labeling of said sequences with <sup>33</sup>P ATP; or using any of said sequences with radiolabeled RNA from both a treated fish and control. Applicants submit Larkin *et al* does not teach nor anticipate each and every limitation of the instant claims. As such Larkin *et al* does not anticipate the instant invention.

In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

### **CONCLUSION**

Applicants respectfully request entry of the foregoing remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 1-32

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define patentable subject matter and is in condition for allowance. Accordingly, Applicant respectfully requests allowance of these claims.

If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at telephone number shown below.

This response is being filed with a petition for a one month extension of time and the required fee. Although, Applicants believe that no extensions of time or fees are required with submission of this paper, Applicants request that this submission also be considered as a petition for any extensions of time if necessary. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,



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